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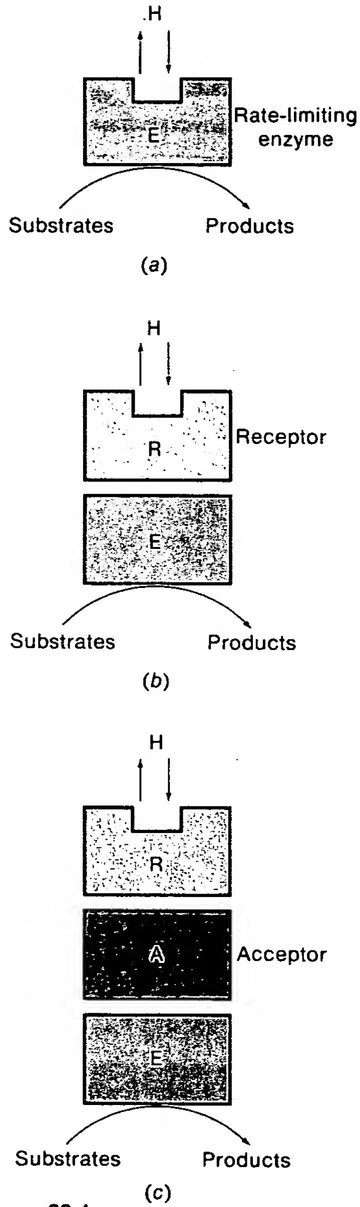

Figure 29-1
Possible mechanisms of hormone action. *(a)* The hormone (H) could theoretically activate an enzyme (E) directly as an allosteric effector. *(b)* Alternatively, there might be a separate binding protein for the hormone, called a receptor (R), which then activates an enzyme. *(c)* Another possibility interposes an acceptor protein (A) between the receptor and enzyme.

The molecular aspects of hormone action are similar to many other processes that involve the relay of extracellular chemical signals into cellular responses. For example, the biochemical distinctions between the action of *pheromones* (that travel between organisms), hormones (that travel between tissues), and neurotransmitters (that travel between cells) are slight; the differences between these classes of chemical stimuli relate largely to the distance they travel. In fact, several compounds that were initially discovered as hormones are now being shown to act as neurotransmitters as well. In addition to the classical hormones, many *polypeptide growth factors* circulate in the blood and act on target cells in a manner analogous to hormones.

It is likely that many of the processes involved in cell differentiation are mediated by hormone-like substances that are secreted by one cell and modify the developmental potential of neighboring or distant cells. That such substances exist is well-established, but they have been difficult to isolate and study because they are present in minute amounts. Nevertheless, analysis of the action of these compounds will likely fit into the intellectual framework of molecular endocrinology. Virus-infected cells synthesize a hormone-like macromolecule called *interferon* that diffuses to neighboring cells and stimulates them to synthesize proteins that will protect them against viral infection. The action of interferon shares many features with hormone action.

HORMONE ACTION IS MEDIATED BY RECEPTORS

Initially it was thought that hormones might bind directly to specific rate-limiting enzymes, thereby either activating or inactivating them (Figure 29-1*a*). However, when this idea was not confirmed experimentally, the concept of a receptor was introduced. *Receptors* are proteins that bind a hormone with high specificity and affinity. *Each hormone binds with high affinity to biochemically distinct receptors. Binding of the hormone induces a conformational change in the receptor, and this change perturbs other macromolecules.* In the simplest scheme, the receptor might be coupled to a rate-limiting enzyme (Figure 29-1*b*). This idea also proved to be too simple, at least for the case that we know most about—namely, the activation of adenylate cyclase. In this case, another protein is interspersed between receptor and rate-limiting enzyme. The protein that is activated by the receptor is called an *acceptor,* and it is responsible for directly mediating enzyme activation (Figure 29-1*c*). All hormones that activate (or inactivate) adenylate cyclase are thought to function by means of receptors and acceptors. However, the molecular mechanism of action of many hormones remains unknown; thus the simpler schemes shown in Figure 29-1 may turn out to be applicable in some hormonal systems. Likewise, more complicated trains of events also may be discovered. Consider the potential advantages and disadvantages of each of the schemes shown in Figure 29-1. Also note that the complexes shown are depicted as permanently coupled. In fact, each of the components is thought to be in equilibrium, perhaps as depicted in Figure 29-2. Now you can see the potential for multiple receptors to impinge on the same acceptors or for different acceptors to have different effects on the same enzyme. Receptors may act catalytically such

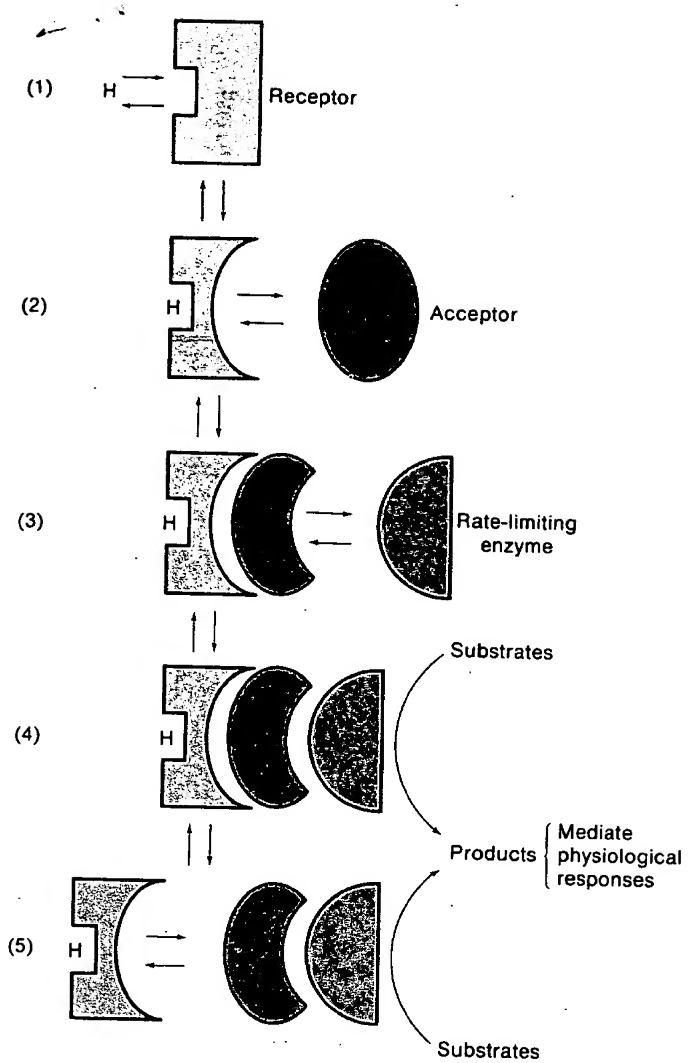

Figure 29-2
Generalized scheme of hormone-receptor action. A hormone (H) plus receptor interact reversibly (1) to produce a hormone-receptor complex (2) with an altered conformation that allows the receptor to interact with an acceptor molecule to form a hormone-receptor-acceptor complex (3). This process activates the acceptor (indicated by another conformational change) so that it can modulate the activity of a rate-limiting step (4) in metabolism or transcription. The activated acceptor may be able to stimulate the enzyme in the absence of the receptor (5) if the receptor acts catalytically.

that one receptor may activate many acceptor molecules. The kinetics of interaction of the various components also may be important for a dynamic control of enzyme activity.

The important point is that *all hormones act by binding to macromolecular receptors that are located either on the cell membrane or inside of responsive cells.* Binding of the hormone induces a conformational change in the receptor; this conformational change perturbs other macromolecules (acceptors) and elicits a chain of events that leads to a vast array of cellular changes ranging from alterations in enzyme activities to changes in gene expression. With time, these effects may lead to profound alterations in cell growth, morphology, and function. A detailed description of the molecular events leading from hormone-receptor binding to activation of rate-limiting enzymes constitutes one of the major goals of molecular endocrinology.

Table 29-1 lists many of the common hormones of vertebrates. Structurally, they range from amino acid derivatives, such as epinephrine and melatonin, to cholesterol-derived steroid hormones, to large polypeptides.